WHAT IS CLAIMED IS:

4 🖶

5 🗒

6 №

7 47

9

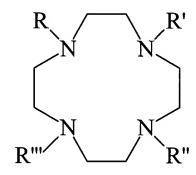
2

3

4

0)

- 1. A contrast agent comprising:
- 2 a tetraazacyclododecane ligand having a general formula as 3 follows:



wherein pendent arms R, R', R'' and R''' are amides having a general formula: $-CR_1H-CO-NH-CH_2-R_2$, wherein R_1 includes organic substituents and R_2 is not hydrogen; and

- a paramagnetic metal ion coordinated to said tetraazacyclododecane ligand.
- 2. The contrast agent as recited in Claim 1 further including a water molecule associated with said tetraazacyclododecane ligand and said paramagnetic metal ion such that said water molecule has a $\Delta\omega \bullet \tau_M \geq 1$.
- 3. The contrast agent as recited in Claim 2 wherein $2 \qquad \text{said } \Delta\omega \, \geq \, 6 \text{ ppm}.$

- 4. The contrast agent as recited in Claim 2 wherein said $5. \quad \text{The contrast agent as recited in Claim 1 wherein said} \\ 2 \quad \text{paramagnetic metal is selected from the group consisting of:} \\ 3 \quad \quad \text{Eu}^{3+}; \\ 4 \quad \quad \text{Tb}^{3+}; \\ 5 \quad \quad \text{Dy}^{3+}; \text{ and} \\ 6 \not\models \text{A} \qquad \quad \text{Ho}^{3+}.$
- 6. The contrast agent as recited in Claim 1 wherein said
 paramagnetic metal is selected from the group consisting of:
- 7. The contrast agent as recited in Claim 1 wherein said $R_2 \ \ \text{does not have a proton exchangeable group.}$
- 8. The contrast agent as recited in Claim 7 wherein said R_2 is selected from the group consisting of:
- 3 Alkyl groups having 20 carbon atoms or less;

Cycloalkyl groups having 20 carbon atoms or less; 4 5 Alkyloxy groups having 20 carbon atoms or less; 6 Alkyl ethers having 10 oxygen atoms or less and 20 carbon atoms or less; and 7 Polyols having 20 carbon atoms or less. 8 9. The contrast agent as recited in Claim 1 wherein said R_1 is selected from the group consisting of: 1 2 3 4 Η; Alkyl groups having 20 carbon atoms or less; Cycloalkyl groups having 20 carbon atoms or less; 5 ຄຸ້ງ Alkyloxy groups having 20 carbon atoms or less; 6 14 Alkyl ethers having 10 oxygen atoms or less and 20 carbon 7 🗓 atoms or less; and Polyols having 20 carbon atoms or less.

2

3

4

5

100

11

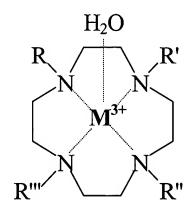
12

13

14

2

subjecting a contrast agent contained within a sample to a radio frequency pulse wherein said contrast agent is a tetraazacyclododecane ligand having a general formula of:



wherein pendent arms R, R', R'' and R''' comprise organic substituents and said tetraazacyclododecane ligand further includes a paramagnetic metal ion (M^{3+}) coordinated to said tetraazacyclododecane ligand and a water molecule (H_2O) associated with said tetraazacyclododecane ligand; and

obtaining a magnetization transfer signal by applying a radio frequency pulse at a resonance frequency of said water molecule.

- 11. The method as recited in Claim 10 wherein said water molecule has a $\Delta\omega\bullet\tau_{M}\,\geq\,1\,.$
 - 12. The method as recited in Claim 10 further includes

- 2 producing a magnetization transfer magnetic resonance image from
- 3 said magnetization transfer signal.
- 13. The method as recited in Claim 10 further includes2 applying said radio frequency pulse as a saturating pulse.
- 14. The method as recited in Claim 10 further includes
 2 said contrast agent with at least one pendent arm containing an
 3 h. amide group.
 - 15. The method as recited in Claim 14 wherein said pendent arms are identical and have the general formula: $-CHR_1-CO-NR_2-R_3, \quad \text{wherein} \quad R_1, \quad R_2 \quad \text{and} \quad R_3 \quad \text{comprise} \quad \text{organic} \quad \text{substituents}.$
- 16. The method as recited in Claim 14 wherein said R_1 and R_2 are R_3 has the general formula: $-(CH_2)_nCOOR_4$
- 3 where

0 2 []

01 3 a

þ4

- n = 1-20; and
- 5 R₄ is selected from the group consisting of:
- 6 H;
- 7 Group IA or IIA metal ions; and
- 8 alkyl groups containing from one to twenty Carbon
- 9 atoms.

```
17.
                    The method as recited in Claim 14 wherein said
 2
       paramagnetic metal ion is selected from the group consisting of:
            Tb^{3+};
 3
            Dy^{3+}; and
 4
            Ho^{3+}.
 5
             18.
                    The method as recited in Claim 14 wherein said
       paramagnetic metal ion is selected from the group consisting of:
 3 4 5
            Eu<sup>3+</sup>;
            Pr3+; and
 5 M
            Nd^{3+}.
  44
  Ļ.
  The method as recited in Claim 14 wherein said
            19.
       R_1 and R_2 are H, and R_3 has the general formula: -
 3
       (CH_2)_nP(O)(OR_4OR_5) where
            n = 1-20;
 4
 5
            said R4 is selected from the group consisting of:
 6
                  H;
 7
                  alkaline earth metal ions of Groups IA or IIA; and
                  alkyl groups containing one to twenty Carbon atoms;
 8
            and said R<sub>5</sub> is selected from the group consisting of:
 9
10
                 H;
                  alkaline earth metal ions of Groups IA or IIA; and
11
```

alkyl groups containing one to twenty Carbon atoms.

- 20. The method as recited in Claim 14 wherein said R_1 and R_2 are H, and R_3 has the general formula: $-(CH_2)_nR_4$ where
- n = 1-20; and

12

þ.

2

O)

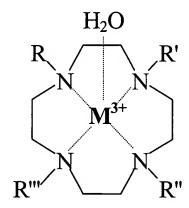
3 III

- 4 R₄ is selected from the group consisting of:
- 5 Pyridine (Py); and
- 6 Phenol (Ph).
 - 21. The method as recited in Claim 14 wherein said pendent arms R and R'' are identical, said pendent arms R' and R''' are identical, and said pendent arms R' and R''' are not equal to said pendent arms R and R''.
- equal to said pendent arms R and R''.

 22. The method as recited in Claim 21 wherein

 said pendent arms R and R'' have the general formula:
- 3 $-CR_1H-CO-NH-CH_2-R_2$; and
- 4 said pendent arms R' and R''' have the general formula:
- 5 -CHR₃-CO-NH-R₄ wherein
- said R₁, R₂, R₃, and R₄ comprise organic substituents; and
- 7 R_2 is not equal to R_4 .
- 23. The method as recited in Claim 14 further
 2 includes obtaining said magnetization transfer signal by

- 3 applying a radio frequency pulse at a resonance frequency of
- 4 said protons associated with said amide.



wherein pendent arms R, R', R'' and R''' comprise

organic substituents and said tetraazacyclododecane ligand

further includes a paramagnetic metal ion (M³+) coordinated to

said tetraazacyclododecane ligand and a water molecule (H2O)

said tetraazacyclododecane ligand and a water molecule (H2O)

make the said tetraazacyclododecane ligand, wherein said

subjected to a radio frequency pulse; and

a magnetic resonance apparatus configured to produce said frequency pulse.

12

13

2

- 25. The magnetic resonance system recited in Claim 24, further comprising a sample containing said MR contrast agent.
- 26. The magnetic resonance system recited in Claim 24, wherein said sample is a living subject.

The magnetic resonance system recited in Claim 24, 27. wherein said magnetic resonance apparatus produces magnetization transfer image of said sample from said magnetization transfer signal.

2

3

4

2

3

THE THE STATE OF

3 44

4 N

6

2

3

4

- 28. The magnetic resonance system recited in Claim 27, wherein said magnetic resonance apparatus produces said magnetization transfer image by applying said radio frequency pulse at a resonance frequency of said water molecule.
- 29. The magnetic resonance system recited in Claim 28, wherein said magnetic resonance apparatus produces a magnetization transfer difference image by applying said radio frequency pulse at a $\Delta \omega$ of said water molecule, acquiring said magnetization transfer signal and subtracting said signal from a MR signal obtained by applying a radio frequency pulse at $-\Delta \omega$.
- 30. The magnetic resonance system recited in Claim 27, wherein said magnetic resonance apparatus produces said magnetization transfer image by applying said radio frequency pulse at a resonance frequency of protons associated with an amide included in one or more of said pendent arms.

31. The magnetic resonance system recited in Claim 24, wherein said radio frequency pulse is produced by said magnetic resonance apparatus and is a saturating pulse.

2

3

2 3

2

- 32. The magnetic resonance system recited in Claim 24,

 wherein said saturating pulse is applied at a resonance

 frequency of said water molecule.
 - 33. The magnetic resonance system recited in Claim 24, wherein said saturating pulse ranges from about 1 to about 3 seconds.
 - 34. The magnetic resonance system recited in Claim 24 wherein said water molecule has a $\Delta\omega\bullet\tau_\text{M}\,\geq\,1\,.$
 - 35. The magnetic resonance system recited in Claim 24 wherein said $\Delta\omega$ \geq 6 ppm.
- 36. The magnetic resonance system recited in Claim 24 wherein said τ_{M} \geq 1 μs .